



COPY OF PAPERS  
ORIGINALLY FILED

SEQUENCE LISTING

<110> Bristol-Myers Squibb Company

<120> AGGRECAN DEGRADING METALLO PROTEASES

<130> DM6909B

<160> 21

<170> PatentIn version 3.0

<210> 1

<211> 4192

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (406)..(2916)

<400> 1

acagacacat atgcacgaga gagacagagg aggaagaga cagagacaaa ggcacagcgg 60

aagaaggcag agacagggca ggcacagaag cggcccagac agagtcctac agagggagag 120

gccagagaag ctgcagaaga cacaggcagg gagagacaaa gatccaggaa aggagggctc 180

aggaggagag tttggagaag ccagaccctt gggcacctct cccaagccca aggactaagt 240

tttctccatt tcctttaacg gtcctcagcc cttctgaaaa ctttgccctct gaccttggca 300

ggagtcgaag cccccaggct acagagagga gctttccaaa gctaggggtgt ggaggacttg 360

gtgccctaga cggcctcagt cctcccagc tgcagtaacca gtgcc atg tcc cag aca 417  
Met Ser Gln Thr  
1

ggc tgc cat ccc ggg agg ggc ttg gca ggg cgc tgg ctg tgg gga gcc 465  
Gly Ser His Pro Gly Arg Gly Leu Ala Gly Arg Trp Leu Trp Gly Ala  
5 10 15 20

caa ccc tgc ctc ctg ctc ccc att gtg ccg ctc tcc tgg ctg gtg tgg 513  
Gln Pro Cys Leu Leu Leu Pro Ile Val Pro Leu Ser Trp Leu Val Trp  
25 30 35

ctg ctt ctg cta ctg ctg gcc tct ctc ctg ccc tca gcc cgg ctg gcc 561  
Leu Leu Leu Leu Leu Ala Ser Leu Leu Pro Ser Ala Arg Leu Ala  
40 45 50

agc ccc ctc ccc cgg gag gag gag atc gtg ttt cca gag aag ctc aac 609

RECEIVED

FEB 22 2002

TECH CENTER 1600/2900

INS  
CI  
B

Ser Pro Leu Pro Arg Glu Glu Glu Ile Val Phe Pro Glu Lys Leu Asn  
 55 60 65  
 ggc agc gtc ctg cct ggc tcg ggc gcc cct gcc agg ctg ttg tgc cgc 657  
 Gly Ser Val Leu Pro Gly Ser Gly Ala Pro Ala Arg Leu Leu Cys Arg  
 70 75 80  
 ttg cag gcc ttt ggg gag acg ctg cta cta gag ctg gag cag gac tcc 705  
 Leu Gln Ala Phe Gly Glu Thr Leu Leu Leu Glu Leu Glu Gln Asp Ser  
 85 90 95 100  
 ggt gtg cag gtc gag ggg ctg aca gtg cag tac ctg ggc cag gcg cct 753  
 Gly Val Gln Val Glu Gly Leu Thr Val Gln Tyr Leu Gly Gln Ala Pro  
 105 110 115  
 gag ctg ctg ggt gga gca gag cct ggc acc tac ctg act ggc acc atc 801  
 Glu Leu Leu Gly Gly Ala Glu Pro Gly Thr Tyr Leu Thr Gly Thr Ile  
 120 125 130  
 aat gga gat ccg gag tcg gtg gca tct ctg cac tgg gat ggg gga gcc 849  
 Asn Gly Asp Pro Glu Ser Val Ala Ser Leu His Trp Asp Gly Gly Ala  
 135 140 145  
 ctg tta ggc gtg tta caa tat cgg ggg gct gaa ctc cac ctc cag ccc 897  
 Leu Leu Gly Val Leu Gln Tyr Arg Gly Ala Glu Leu His Leu Gln Pro  
 150 155 160  
 ctg gag gga ggc acc cct aac tct gct ggg gga cct ggg gct cac atc 945  
 Leu Glu Gly Gly Thr Pro Asn Ser Ala Gly Gly Pro Gly Ala His Ile  
 165 170 175 180  
 cta cgc cgg aag agt cct gcc agc ggt caa ggt ccc atg tgc aac gtc 993  
 Leu Arg Arg Lys Ser Pro Ala Ser Gly Gln Gly Pro Met Cys Asn Val  
 185 190 195  
 aag gct cct ctt gga agc ccc agc ccc aga ccc cga aga gcc aag cgc 1041  
 Lys Ala Pro Leu Gly Ser Pro Ser Pro Arg Pro Arg Arg Ala Lys Arg  
 200 205 210  
 ttt gct tca ctg agt aga ttt gtg gag aca ctg gtg gtg gca gat gac 1089  
 Phe Ala Ser Leu Ser Arg Phe Val Glu Thr Leu Val Val Ala Asp Asp  
 215 220 225  
 aag atg gcc gca ttc cac ggt gcg ggg cta aag cgc tac ctg cta aca 1137  
 Lys Met Ala Ala Phe His Gly Ala Gly Leu Lys Arg Tyr Leu Leu Thr  
 230 235 240  
 gtg atg gca gca gca gcc aag gcc ttc aag cac cca agc atc cgc aat 1185  
 Val Met Ala Ala Ala Ala Lys Ala Phe Lys His Pro Ser Ile Arg Asn  
 245 250 255 260  
 cct gtc agc ttg gtg gtg act cgg cta gtg atc ctg ggg tca ggc gag 1233  
 Pro Val Ser Leu Val Val Thr Arg Leu Val Ile Leu Gly Ser Gly Glu  
 265 270 275  
 gag ggg ccc caa gtg ggg ccc agt gct gcc cag acc ctg cgc agc ttc 1281  
 Glu Gly Pro Gln Val Gly Pro Ser Ala Ala Gln Thr Leu Arg Ser Phe

INS  
C1

INS  
C1

280	285	290	
tgt gcc tgg cag cgg ggc ctc aac acc cct gag gac tcg gac cct gac			1329
Cys Ala Trp Gln Arg Gly Leu Asn Thr Pro Glu Asp Ser Asp Pro Asp			
295	300	305	
cac ttt gac aca gcc att ctg ttt acc cgt cag gac ctg tgt gga gtc			1377
His Phe Asp Thr Ala Ile Leu Phe Thr Arg Gln Asp Leu Cys Gly Val			
310	315	320	
tcc act tgc gac acg ctg ggt atg gct gat gtg ggc acc gtc tgt gac			1425
Ser Thr Cys Asp Thr Leu Gly Met Ala Asp Val Gly Thr Val Cys Asp			
325	330	335	340
ccg gct cgg agc tgt gcc att gtg gag gat gat ggg ctc cag tca gcc			1473
Pro Ala Arg Ser Cys Ala Ile Val Glu Asp Asp Gly Leu Gln Ser Ala			
345	350	355	
ttc act gct gct cat gaa ctg ggt cat gtc ttc aac atg ctc cat gac			1521
Phe Thr Ala Ala His Glu Leu Gly His Val Phe Asn Met Leu His Asp			
360	365	370	
aac tcc aag cca tgc atc agt ttg aat ggg cct ttg agc acc tct cgc			1569
Asn Ser Lys Pro Cys Ile Ser Leu Asn Gly Pro Leu Ser Thr Ser Arg			
375	380	385	
cat gtc atg gcc cct gtg atg gct cat gtg gat cct gag gag ccc tgg			1617
His Val Met Ala Pro Val Met Ala His Val Asp Pro Glu Glu Pro Trp			
390	395	400	
tcc ccc tgc agt gcc cgc ttc atc act gac ttc ctg gac aat ggc tat			1665
Ser Pro Cys Ser Ala Arg Phe Ile Thr Asp Phe Leu Asp Asn Gly Tyr			
405	410	415	420
ggg cac tgt ctc tta gac aaa cca gag gct cca ttg cat ctg cct gtg			1713
Gly His Cys Leu Leu Asp Lys Pro Glu Ala Pro Leu His Leu Pro Val			
425	430	435	
act ttc cct ggc aag gac tat gat gct gac cgc cag tgc cag ctg acc			1761
Thr Phe Pro Gly Lys Asp Tyr Asp Ala Asp Arg Gln Cys Gln Leu Thr			
440	445	450	
ttc ggg ccc gac tca cgc cat tgt cca cag ctg ccg ccg ccc tgt gct			1809
Phe Gly Pro Asp Ser Arg His Cys Pro Gln Leu Pro Pro Pro Cys Ala			
455	460	465	
gcc ctc tgg tgc tct ggc cac ctc aat ggc cat gcc atg tgc cag acc			1857
Ala Leu Trp Cys Ser Gly His Leu Asn Gly His Ala Met Cys Gln Thr			
470	475	480	
aaa cac tcg ccc tgg gcc gat ggc aca ccc tgc ggg ccc gca cag gcc			1905
Lys His Ser Pro Trp Ala Asp Gly Thr Pro Cys Gly Pro Ala Gln Ala			
485	490	495	500
tgc atg ggt ggt cgc tgc ctc cac atg gac cag ctc cag gac ttc aat			1953
Cys Met Gly Gly Arg Cys Leu His Met Asp Gln Leu Gln Asp Phe Asn			
505	510	515	

att cca cag gct ggt ggc tgg ggt cct tgg gga cca tgg ggt gac tgc 2001  
 Ile Pro Gln Ala Gly Gly Trp Gly Pro Trp Gly Pro Trp Gly Asp Cys  
 520 525 530  
 tct cgg acc tgt ggg ggt ggt gtc cag ttc tcc tcc cga gac tgc acg 2049  
 Ser Arg Thr Cys Gly Gly Gly Val Gln Phe Ser Ser Arg Asp Cys Thr  
 535 540 545  
 agg cct gtc ccc cgg aat ggt ggc aag tac tgt gag ggc cgc cgt acc 2097  
 Arg Pro Val Pro Arg Asn Gly Gly Lys Tyr Cys Glu Gly Arg Arg Thr  
 550 555 560  
 cgc ttc cgc tcc tgc aac act gag gac tgc cca act ggc tca gcc ctg 2145  
 Arg Phe Arg Ser Cys Asn Thr Glu Asp Cys Pro Thr Gly Ser Ala Leu  
 565 570 575 580  
 acc ttc cgc gag gag cag tgt gct gcc tac aac cac cgc acc gac ctc 2193  
 Thr Phe Arg Glu Glu Gln Cys Ala Ala Tyr Asn His Arg Thr Asp Leu  
 585 590 595  
 ttc aag agc ttc cca ggg ccc atg gac tgg gtt cct cgc tac aca ggc 2241  
 Phe Lys Ser Phe Pro Gly Pro Met Asp Trp Val Pro Arg Tyr Thr Gly  
 600 605 610  
 gtg gcc ccc cag gac cag tgc aaa ctc acc tgc cag gcc cgg gca ctg 2289  
 Val Ala Pro Gln Asp Gln Cys Lys Leu Thr Cys Gln Ala Arg Ala Leu  
 615 620 625  
 ggc tac tac tat gtg ctg gag cca cgg gtg gta gat ggg acc ccc tgt 2337  
 Gly Tyr Tyr Tyr Val Leu Glu Pro Arg Val Val Asp Gly Thr Pro Cys  
 630 635 640  
 tcc ccg gac agc tcc tcg gtc tgt gtc cag ggc cga tgc atc cat gct 2385  
 Ser Pro Asp Ser Ser Val Cys Val Gln Gly Arg Cys Ile His Ala  
 645 650 655 660  
 ggc tgt gat cgc atc att ggc tcc aag aag aag ttt gac aag tgc atg 2433  
 Gly Cys Asp Arg Ile Ile Gly Ser Lys Lys Lys Phe Asp Lys Cys Met  
 665 670 675  
 gtg tgc gga ggg gac ggt tct ggt tgc agc aag cag tca ggc tcc ttc 2481  
 Val Cys Gly Gly Asp Gly Ser Gly Cys Ser Lys Gln Ser Gly Ser Phe  
 680 685 690  
 agg aaa ttc agg tac gga tac aac aat gtg gtc act atc ccc gcg ggg 2529  
 Arg Lys Phe Arg Tyr Gly Tyr Asn Asn Val Val Thr Ile Pro Ala Gly  
 695 700 705  
 gcc acc cac att ctt gtc cgg cag cag gga aac cct ggc cac cgg agc 2577  
 Ala Thr His Ile Leu Val Arg Gln Gln Gly Asn Pro Gly His Arg Ser  
 710 715 720  
 atc tac ttg gcc ctg aag ctg cca gat ggc tcc tat gcc ctc aat ggt 2625  
 Ile Tyr Leu Ala Leu Lys Leu Pro Asp Gly Ser Tyr Ala Leu Asn Gly  
 725 730 735 740

125  
 101

gaa tac acg ctg atg ccc tcc ccc aca gat gtg gta ctg cct ggg gca 2673  
 Glu Tyr Thr Leu Met Pro Ser Pro Thr Asp Val Val Leu Pro Gly Ala  
 745 750 755  
 gtc agc ttg cgc tac agc ggg gcc act gca gcc tca gag aca ctg tca 2721  
 Val Ser Leu Arg Tyr Ser Gly Ala Thr Ala Ala Ser Glu Thr Leu Ser  
 760 765 770  
 ggc cat ggg cca ctg gcc cag cct ttg aca ctg caa gtc cta gtg gct 2769  
 Gly His Gly Pro Deu Ala Gln Pro Leu Thr Leu Gln Val Leu Val Ala  
 775 780 785  
 ggc aac ccc cag gac aca cgc ctc cga tac agc ttc ttc gtg ccc cgg 2817  
 Gly Asn Pro Gln Asp Thr Arg Leu Arg Tyr Ser Phe Phe Val Pro Arg  
 790 795 800  
 ccg acc cct tca acg cca cgc ccc act ccc cag gac tgg ctg cac cga 2865  
 Pro Thr Pro Ser Thr Pro Arg Pro Thr Pro Gln Asp Trp Leu His Arg  
 805 810 815 820  
 aga gca cag att ctg gag atc ctt cgg cgg cgc ccc tgg gcg ggc agg 2913  
 Arg Ala Gln Ile Leu Glu Ile Leu Arg Arg Arg Pro Trp Ala Gly Arg  
 825 830 835  
 aaa taacctcact atccccggctg ccctttctgg gcaccggggc ctgggactta 2966  
 Lys  
 gctgggagaa agagagagct tctgttgctg cctcatgcta agactcagtg gggaggggct 3026  
 gtgggcgtga gacctgcccc tcctctctgc cctaattgagc aggttgggcc tgccctgggt 3086  
 tcctgccttg ggaggcagt atgggttagt ggatggaagg ggctgacaga cagccctcca 3146  
 tctaaactgc cccctctgcc ctgcgggtca caggagggag ggggaaggca gggagggcct 3206  
 gggccccagt tgtatttatt tagtatttat tcaactttat ttagcaccag ggaaggggac 3266  
 aaggactagg gtccctgggga acctgacccc tgaccctca tagccctcac cctggggcta 3326  
 ggaaatccag ggtggtggtg ataggtataa gtggtgtgtg tatgcgtgtg tgtgtgtgtg 3386  
 tgaaaatgtg tgtgtgctta tgtatgaggt acaacctgtt ctgctttct cttcctgaat 3446  
 tttatTTTTT gggaaaagaa aagtcaagg taggggtggc cttcagggag tgagggatta 3506  
 tcctTTTTTT tttctttctt tctttctttt tttttttgag acagaatctc gctctgtcgc 3566  
 ccaggctgga gtgcaatggc acaatctcgg ctactgcat cctccgctc cggggttcaa 3626  
 gtgattctca tgccctagcc tcctgagtag ctgggattac aggtcctgc caccagccc 3686  
 ggctaatttt tgttttgttt tgtttggaga cagagtctcg ctattgtcac cagggttgga 3746  
 atgatttcag ctactgcaa ccttcgccac ctgggttcca gcaattctcc tgccctagcc 3806  
 tcccagtag ctgagattat aggcacctac caccagccc ggctaatttt tgtattttta 3866

INS  
C1

gtagagacgg ggtttcacca tgttggccag gctggtctcg aactcctgac cttaggtgat 3926  
 ccaactgcct tcattctcca aagtgtggg attacaggcg tgagccaccg tgcctggcca 3986  
 cgcccaacta atttttgtat ttttagtaga gacagggttt caccatgttg gccaggctgc 4046  
 tcttgaactc ctgacctcag gtaatcgacc tgcctcgcc tcccaaagtg ctgggattac 4106  
 aggtgtgagc caccacgccc ggtacatatt ttttaaattg aattctacta tttatgtgat 4166  
 ccttttggag tcagacagat gtgggt 4192

<210> 2

<211> 837

<212> PRT

<213> Homo sapiens

<400> 2

Met Ser Gln Thr Gly Ser His Pro Gly Arg Gly Leu Ala Gly Arg Trp  
 1 5 10 15  
 Leu Trp Gly Ala Gln Pro Cys Leu Leu Leu Pro Ile Val Pro Leu Ser  
 20 25 30  
 Trp Leu Val Trp Leu Leu Leu Leu Leu Ala Ser Leu Leu Pro Ser  
 35 40 45  
 Ala Arg Leu Ala Ser Pro Leu Pro Arg Glu Glu Glu Ile Val Phe Pro  
 50 55 60  
 Glu Lys Leu Asn Gly Ser Val Leu Pro Gly Ser Gly Ala Pro Ala Arg  
 65 70 75 80  
 Leu Leu Cys Arg Leu Gln Ala Phe Gly Glu Thr Leu Leu Leu Glu Leu  
 85 90 95  
 Glu Gln Asp Ser Gly Val Gln Val Glu Gly Leu Thr Val Gln Tyr Leu  
 100 105 110  
 Gly Gln Ala Pro Glu Leu Leu Gly Gly Ala Glu Pro Gly Thr Tyr Leu  
 115 120 125  
 Thr Gly Thr Ile Asn Gly Asp Pro Glu Ser Val Ala Ser Leu His Trp  
 130 135 140  
 Asp Gly Gly Ala Leu Leu Gly Val Leu Gln Tyr Arg Gly Ala Glu Leu  
 145 150 155 160  
 His Leu Gln Pro Leu Glu Gly Gly Thr Pro Asn Ser Ala Gly Gly Pro  
 165 170 175  
 Gly Ala His Ile Leu Arg Arg Lys Ser Pro Ala Ser Gly Gln Gly Pro

INS  
C1

INS  
C1

180					185					190					
Met	Cys	Asn	Val	Lys	Ala	Pro	Leu	Gly	Ser	Pro	Ser	Pro	Arg	Pro	Arg
	195						200					205			
Arg	Ala	Lys	Arg	Phe	Ala	Ser	Leu	Ser	Arg	Phe	Val	Glu	Thr	Leu	Val
	210					215					220				
Val	Ala	Asp	Asp	Lys	Met	Ala	Ala	Phe	His	Gly	Ala	Gly	Leu	Lys	Arg
225					230					235					240
Tyr	Leu	Leu	Thr	Val	Met	Ala	Ala	Ala	Ala	Lys	Ala	Phe	Lys	His	Pro
			245							250				255	
Ser	Ile	Arg	Asn	Pro	Val	Ser	Leu	Val	Val	Thr	Arg	Leu	Val	Ile	Leu
			260							265				270	
Gly	Ser	Gly	Glu	Glu	Gly	Pro	Gln	Val	Gly	Pro	Ser	Ala	Ala	Gln	Thr
			275				280					285			
Leu	Arg	Ser	Phe	Cys	Ala	Trp	Gln	Arg	Gly	Leu	Asn	Thr	Pro	Glu	Asp
	290					295					300				
Ser	Asp	Pro	Asp	His	Phe	Asp	Thr	Ala	Ile	Leu	Phe	Thr	Arg	Gln	Asp
305					310					315					320
Leu	Cys	Gly	Val	Ser	Thr	Cys	Asp	Thr	Leu	Gly	Met	Ala	Asp	Val	Gly
				325					330					335	
Thr	Val	Cys	Asp	Pro	Ala	Arg	Ser	Cys	Ala	Ile	Val	Glu	Asp	Asp	Gly
			340					345					350		
Leu	Gln	Ser	Ala	Phe	Thr	Ala	Ala	His	Glu	Leu	Gly	His	Val	Phe	Asn
	355						360					365			
Met	Leu	His	Asp	Asn	Ser	Lys	Pro	Cys	Ile	Ser	Leu	Asn	Gly	Pro	Leu
	370					375					380				
Ser	Thr	Ser	Arg	His	Val	Met	Ala	Pro	Val	Met	Ala	His	Val	Asp	Pro
385					390					395					400
Glu	Glu	Pro	Trp	Ser	Pro	Cys	Ser	Ala	Arg	Phe	Ile	Thr	Asp	Phe	Leu
				405					410					415	
Asp	Asn	Gly	Tyr	Gly	His	Cys	Leu	Leu	Asp	Lys	Pro	Glu	Ala	Pro	Leu
		420						425					430		
His	Leu	Pro	Val	Thr	Phe	Pro	Gly	Lys	Asp	Tyr	Asp	Ala	Asp	Arg	Gln
	435						440					445			
Cys	Gln	Leu	Thr	Phe	Gly	Pro	Asp	Ser	Arg	His	Cys	Pro	Gln	Leu	Pro
	450					455					460				
Pro	Pro	Cys	Ala	Ala	Leu	Trp	Cys	Ser	Gly	His	Leu	Asn	Gly	His	Ala
465					470					475					480
Met	Cys	Gln	Thr	Lys	His	Ser	Pro	Trp	Ala	Asp	Gly	Thr	Pro	Cys	Gly

485 490 495  
 Pro Ala Gln Ala Cys Met Gly Gly Arg Cys Leu His Met Asp Gln Leu  
 500 505 510  
 Gln Asp Phe Asn Ile Pro Gln Ala Gly Gly Trp Gly Pro Trp Gly Pro  
 515 520 525  
 Trp Gly Asp Cys Ser Arg Thr Cys Gly Gly Gly Val Gln Phe Ser Ser  
 530 535 540  
 Arg Asp Cys Thr Arg Pro Val Pro Arg Asn Gly Gly Lys Tyr Cys Glu  
 545 550 555 560  
 Gly Arg Arg Thr Arg Phe Arg Ser Cys Asn Thr Glu Asp Cys Pro Thr  
 565 570 575  
 Gly Ser Ala Leu Thr Phe Arg Glu Glu Gln Cys Ala Ala Tyr Asn His  
 580 585 590  
 Arg Thr Asp Leu Phe Lys Ser Phe Pro Gly Pro Met Asp Trp Val Pro  
 595 600 605  
 Arg Tyr Thr Gly Val Ala Pro Gln Asp Gln Cys Lys Leu Thr Cys Gln  
 610 615 620  
 Ala Arg Ala Leu Gly Tyr Tyr Tyr Val Leu Glu Pro Arg Val Val Asp  
 625 630 635 640  
 Gly Thr Pro Cys Ser Pro Asp Ser Ser Ser Val Cys Val Gln Gly Arg  
 645 650 655  
 Cys Ile His Ala Gly Cys Asp Arg Ile Ile Gly Ser Lys Lys Lys Phe  
 660 665 670  
 Asp Lys Cys Met Val Cys Gly Gly Asp Gly Ser Gly Cys Ser Lys Gln  
 675 680 685  
 Ser Gly Ser Phe Arg Lys Phe Arg Tyr Gly Tyr Asn Asn Val Val Thr  
 690 695 700  
 Ile Pro Ala Gly Ala Thr His Ile Leu Val Arg Gln Gln Gly Asn Pro  
 705 710 715 720  
 Gly His Arg Ser Ile Tyr Leu Ala Leu Lys Leu Pro Asp Gly Ser Tyr  
 725 730 735  
 Ala Leu Asn Gly Glu Tyr Thr Leu Met Pro Ser Pro Thr Asp Val Val  
 740 745 750  
 Leu Pro Gly Ala Val Ser Leu Arg Tyr Ser Gly Ala Thr Ala Ala Ser  
 755 760 765  
 Glu Thr Leu Ser Gly His Gly Pro Leu Ala Gln Pro Leu Thr Leu Gln  
 770 775 780  
 Val Leu Val Ala Gly Asn Pro Gln Asp Thr Arg Leu Arg Tyr Ser Phe

INS  
C1

785                      790                      795                      800

Phe Val Pro Arg Pro Thr Pro Ser Thr Pro Arg Pro Thr Pro Gln Asp  
                                  805                      810                      815

Trp Leu His Arg Arg Ala Gln Ile Leu Glu Ile Leu Arg Arg Arg Pro  
                                  820                      825                      830

Trp Ala Gly Arg Lys  
                                  835

<210> 4

<211> 26

<212> PRT

<213> Bos taurus

<400> 4

Phe Ala Ser Leu Ser Arg Val Glu Thr Leu Val Val Ala Asp Asp Lys  
   1                                 5                                 10                                 15

Met Ala Ala Phe His Gly Ala Gly Leu Lys  
                                  20                                 25

<210> 5

<211> 7

<212> PRT

<213> Bos taurus

<400> 5

Tyr Thr Gly Val Ala Pro Arg  
   1                                 5

<210> 6

<211> 11

<212> PRT

<213> Bos taurus

<400> 6

Ala Leu Gly Tyr Tyr Tyr Val Leu Asp Pro Arg  
   1                                 5                                 10

<210> 7

<211> 21

INS  
 1/21

<212> DNA

<213> Mus musculus

<400> 7

gggggtggtg tccagttctc c

21

<210> 8

<211> 23

<212> DNA

<213> Mus musculus

<400> 8

ggccctggaa agctcttgaa gag

23

<210> 9

<211> 23

<212> DNA

<213> Homo sapiens

<400> 9

ccccggaatg gtggcaagta ctg

23

<210> 10

<211> 23

<212> DNA

<213> Homo sapiens

<400> 10

acccacatct gtctgactcc aaa

23

<210> 11

<211> 23

<212> DNA

<213> Homo sapiens

<400> 11

ccagttgggc agtcctcagt gtt

23

<210> 12

<211> 22

<212> DNA

105  
C1

<213> Homo sapiens

<400> 12

ggtcgggtgog gtggtttag gc

22

<210> 13

<211> 17

<212> PRT

<213> Homo sapiens

<400> 13

Cys Ala Ser Leu Ser Arg Phe Val Glu Thr Leu Val Val Ala Asp Asp  
1 5 10 15

Lys

<210> 14

<211> 3250

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (121)..(2910)

<400> 14

tgactcaatc ctgcaagcaa gtgtgtgtgt gtcccatcc cccgcccgt taacttcata 60

gcaaataaca aatacccata aagteccagt cgcgcagccc ctcccgcgg gcagcgcaact 120

atg ctg ctc ggg tgg gcg tcc ctg ctg ctg tgc gcg ttc cgc ctg ccc 168  
Met Leu Leu Gly Trp Ala Ser Leu Leu Leu Cys Ala Phe Arg Leu Pro  
1 5 10 15

ctg gcc gcg gtc ggc ccc gcc gcg aca cct gcc cag gat aaa gcc ggg 216  
Leu Ala Ala Val Gly Pro Ala Ala Thr Pro Ala Gln Asp Lys Ala Gly  
20 25 30

cag cct ccg act gct gca gca gcc gcc cag ccc cgc cgg cgg cag ggg 264  
Gln Pro Pro Thr Ala Ala Ala Ala Gln Pro Arg Arg Arg Gln Gly  
35 40 45

gag gag gtg cag gag cga gcc gag cct ccc ggc cac ccg cac ccc ctg 312  
Glu Glu Val Gln Glu Arg Ala Glu Pro Pro Gly His Pro His Pro Leu  
50 55 60

gcg cag cgg cgc agg agc aag ggg ctg gtg cag aac atc gac caa ctc 360

INS  
C1

Ala Gln Arg Arg Arg Ser Lys Gly Leu Val Gln Asn Ile Asp Gln Leu  
 65 70 75 80  
 tac tcc ggc ggc ggc aag gtg ggc tac ctc gtc tac gcg ggc ggc cgg 408  
 Tyr Ser Gly Gly Gly Lys Val Gly Tyr Leu Val Tyr Ala Gly Gly Arg  
 85 90 95  
 agg ttc ctc ttg gac ctg gag cga gat ggt tgc gtg ggc att gct ggc 456  
 Arg Phe Leu Leu Asp Leu Glu Arg Asp Gly Ser Val Gly Ile Ala Gly  
 100 105 110  
 ttc gtg ccc gca gga ggc ggg acg agt gcg ccc tgg cgc cac cgg agc 504  
 Phe Val Pro Ala Gly Gly Gly Thr Ser Ala Pro Trp Arg His Arg Ser  
 115 120 125  
 cac tgc ttc tat cgg ggc aca gtg gac gct agt ccc cgc tct ctg gct 552  
 His Cys Phe Tyr Arg Gly Thr Val Asp Ala Ser Pro Arg Ser Leu Ala  
 130 135 140  
 gtc ttt gac ctc tgt ggg ggt ctc gac ggc ttc ttc gcg gtc aag cac 600  
 Val Phe Asp Leu Cys Gly Gly Leu Asp Gly Phe Phe Ala Val Lys His  
 145 150 155 160  
 gcg cgc tac acc cta aag cca ctg ctg cgc gga ccc tgg gcg gag gaa 648  
 Ala Arg Tyr Thr Leu Lys Pro Leu Leu Arg Gly Pro Trp Ala Glu Glu  
 165 170 175  
 gaa aag ggg cgc gtg tac ggg gat ggg tcc gca cgg atc ctg cac gtc 696  
 Glu Lys Gly Arg Val Tyr Gly Asp Gly Ser Ala Arg Ile Leu His Val  
 180 185 190  
 tac acc cgc gag ggc ttc agc ttc gag gcc ctg ccg ccg cgc gcc agc 744  
 Tyr Thr Arg Glu Gly Phe Ser Phe Glu Ala Leu Pro Pro Arg Ala Ser  
 195 200 205  
 tgc gaa acc ccc gcg tcc aca ccg gag gcc cac gag cat gct ccg gcg 792  
 Cys Glu Thr Pro Ala Ser Thr Pro Glu Ala His Glu His Ala Pro Ala  
 210 215 220  
 cac agc aac ccg agc gga cgc gca gca ctg gcc tgc cag ctc ttg gac 840  
 His Ser Asn Pro Ser Gly Arg Ala Ala Leu Ala Ser Gln Leu Leu Asp  
 225 230 235 240  
 cag tcc gct ctc tgc ccc gct ggg ggc tca gga ccg cag acg tgg tgg 888  
 Gln Ser Ala Leu Ser Pro Ala Gly Gly Ser Gly Pro Gln Thr Trp Trp  
 245 250 255  
 cgg cgg cgg cgc cgc tcc atc tcc ccg gcc cgc cag gtg gag ctg ctt 936  
 Arg Arg Arg Arg Arg Ser Ile Ser Arg Ala Arg Gln Val Glu Leu Leu  
 260 265 270  
 ctg gtg gct gac gcg tcc atg gcg ccg ttg tat ggc cgg ggc ctg cag 984  
 Leu Val Ala Asp Ala Ser Met Ala Arg Leu Tyr Gly Arg Gly Leu Gln  
 275 280 285  
 cat tac ctg ctg acc ctg gcc tcc atc gcc aat agg ctg tac agc cat 1032  
 His Tyr Leu Leu Thr Leu Ala Ser Ile Ala Asn Arg Leu Tyr Ser His

INS  
C1

290 295 300

gct agc atc gag aac cac atc cgc ctg gcc gtg gtg aag gtg gtg gtg 1080  
Ala Ser Ile Glu Asn His Ile Arg Leu Ala Val Val Lys Val Val Val  
305 310 315 320

cta ggc gac aag gac aag agc ctg gaa gtg agc aag aac gct gcc acc 1128  
Leu Gly Asp Lys Asp Lys Ser Leu Glu Val Ser Lys Asn Ala Ala Thr  
325 330 335

aca ctc aag aac ttt tgc aag tgg cag cac caa cac aac cag ctg gga 1176  
Thr Leu Lys Asn Phe Cys Lys Trp Gln His Gln His Asn Gln Leu Gly  
340 345 350

gat gac cat gag gag cac tac gat gca gct atc ctg ttt act cgg gag 1224  
Asp Asp His Glu Glu His Tyr Asp Ala Ala Ile Leu Phe Thr Arg Glu  
355 360 365

gat tta tgt ggg cat cat tca tgt gac acc ctg gga atg gca gac gtt 1272  
Asp Leu Cys Gly His His Ser Cys Asp Thr Leu Gly Met Ala Asp Val  
370 375 380

ggg acc ata tgt tct cca gag cgc agc tgt gct gtg att gaa gac gat 1320  
Gly Thr Ile Cys Ser Pro Glu Arg Ser Cys Ala Val Ile Glu Asp Asp  
385 390 395 400

ggc ctc cac gca gcc ttc act gtg gct cac gaa atc gga cat tta ctt 1368  
Gly Leu His Ala Ala Phe Thr Val Ala His Glu Ile Gly His Leu Leu  
405 410 415

ggc ctc tcc cat gac gat tcc aaa ttc tgt gaa gag acc ttt ggt tcc 1416  
Gly Leu Ser His Asp Asp Ser Lys Phe Cys Glu Glu Thr Phe Gly Ser  
420 425 430

aca gaa gat aag cgc tta atg tct tcc atc ctt acc agc att gat gca 1464  
Thr Glu Asp Lys Arg Leu Met Ser Ser Ile Leu Thr Ser Ile Asp Ala  
435 440 445

tct aag ccc tgg tcc aaa tgc act tca gcc acc atc aca gaa ttc ctg 1512  
Ser Lys Pro Trp Ser Lys Cys Thr Ser Ala Thr Ile Thr Glu Phe Leu  
450 455 460

gat gat ggc cat ggt aac tgt ttg ctg gac cta cca cga aag cag atc 1560  
Asp Asp Gly His Gly Asn Cys Leu Leu Asp Leu Pro Arg Lys Gln Ile  
465 470 475 480

ctg ggc ccc gaa gaa ctc cca gga cag acc tac gat gcc acc cag cag 1608  
Leu Gly Pro Glu Glu Leu Pro Gly Gln Thr Tyr Asp Ala Thr Gln Gln  
485 490 495

tgc aac ctg aca ttc ggg cct gag tac tcc gtg tgt ccc ggc atg gat 1656  
Cys Asn Leu Thr Phe Gly Pro Glu Tyr Ser Val Cys Pro Gly Met Asp  
500 505 510

gtc tgt gct cgc ctg tgg tgt gct gtg gta cgc cag ggc cag atg gtc 1704  
Val Cys Ala Arg Leu Trp Cys Ala Val Val Arg Gln Gly Gln Met Val  
515 520 525

INS  
CI

1752  
tgt ctg acc aag aag ctg cct gcg gtg gaa ggg acg cct tgt gga aag  
Cys Leu Thr Lys Lys Leu Pro Ala Val Glu Gly Thr Pro Cys Gly Lys  
530 535 540

1800  
ggg aga atc tgc ctg cag ggc aaa tgt gtg gac aaa acc aag aaa aaa  
Gly Arg Ile Cys Leu Gln Gly Lys Cys Val Asp Lys Thr Lys Lys Lys  
545 550 555 560

1848  
tat tat tca acg tca agc cat ggc aac tgg gga tct tgg gga tcc tgg  
Tyr Tyr Ser Thr Ser Ser His Gly Asn Trp Gly Ser Trp Gly Ser Trp  
565 570 575

1896  
ggc cag tgt tct cgc tca tgt gga gga gga gtg cag ttt gcc tat cgt  
Gly Gln Cys Ser Arg Ser Cys Gly Gly Val Gln Phe Ala Tyr Arg  
580 585 590

1944  
cac tgt aat aac cct gct ccc aga aac aac gga cgc tac tgc aca ggg  
His Cys Asn Asn Pro Ala Pro Arg Asn Asn Gly Arg Tyr Cys Thr Gly  
595 600 605

1992  
aag agg gcc atc tac cgc tcc tgc agt ctc atg ccc tgc cca ccc aat  
Lys Arg Ala Ile Tyr Arg Ser Cys Ser Leu Met Pro Cys Pro Pro Asn  
610 615 620

2040  
ggt aaa tca ttt cgt cat gaa cag tgt gag gcc aaa aat ggc tat cag  
Gly Lys Ser Phe Arg His Glu Gln Cys Glu Ala Lys Asn Gly Tyr Gln  
625 630 635 640

2088  
tct gat gca aaa gga gtc aaa act ttt gtg gaa tgg gtt ccc aaa tat  
Ser Asp Ala Lys Gly Val Lys Thr Phe Val Glu Trp Val Pro Lys Tyr  
645 650 655

2136  
gca ggt gtc ctg cca gcg gat gtg tgc aag ctg acc tgc aga gcc aag  
Ala Gly Val Leu Pro Ala Asp Val Cys Lys Leu Thr Cys Arg Ala Lys  
660 665 670

2184  
ggc act ggc tac tat gtg gta ttt tct cca aag gtg acc gat ggc act  
Gly Thr Gly Tyr Tyr Val Val Phe Ser Pro Lys Val Thr Asp Gly Thr  
675 680 685

2232  
gaa tgt agg ccg tac agt aat tcc gtc tgc gtc cgg ggg aag tgt gtg  
Glu Cys Arg Pro Tyr Ser Asn Ser Val Cys Val Arg Gly Lys Cys Val  
690 695 700

2280  
aga act ggc tgt gac ggc atc att ggc tca aag ctg cag tat gac aag  
Arg Thr Gly Cys Asp Gly Ile Ile Gly Ser Lys Leu Gln Tyr Asp Lys  
705 710 715 720

2328  
tgc gga gta tgt gga gga gac aac tcc agc tgt aca aag att gtt gga  
Cys Gly Val Cys Gly Gly Asp Asn Ser Ser Cys Thr Lys Ile Val Gly  
725 730 735

2376  
acc ttt aat aag aaa agt aag ggt tac act gac gtg gtg agg att cct  
Thr Phe Asn Lys Lys Ser Lys Gly Tyr Thr Asp Val Val Arg Ile Pro  
740 745 750

INS  
CI

gaa ggg gca acc cac ata aaa gtt cga cag ttc aaa gcc aaa gac cag 2424  
 Glu Gly Ala Thr His Ile Lys Val Arg Gln Phe Lys Ala Lys Asp Gln  
 755 760 765  
 act aga ttc act gcc tat tta gcc ctg aaa aag aaa aac ggt gag tac 2472  
 Thr Arg Phe Thr Ala Tyr Leu Ala Leu Lys Lys Lys Asn Gly Glu Tyr  
 770 775 780  
 ctt atc aat gga aag tac atg atc tcc act tca gag act atc att gac 2520  
 Leu Ile Asn Gly Lys Tyr Met Ile Ser Thr Ser Glu Thr Ile Ile Asp  
 785 790 795 800  
 atc aat gga aca gtc atg aac tat agc ggt tgg agc cac agg gat gac 2568  
 Ile Asn Gly Thr Val Met Asn Tyr Ser Gly Trp Ser His Arg Asp Asp  
 805 810 815  
 ttc ctg cat ggc atg ggc tac tct gcc acg aag gaa att cta ata gtg 2616  
 Phe Leu His Gly Met Gly Tyr Ser Ala Thr Lys Glu Ile Leu Ile Val  
 820 825 830  
 cag att ctt gca aca gac ccc act aaa cca tta gat gtc cgt tat agc 2664  
 Gln Ile Leu Ala Thr Asp Pro Thr Lys Pro Leu Asp Val Arg Tyr Ser  
 835 840 845  
 ttt ttt gtt ccc aag aag tcc act cca aaa gta aac tct gtc act agt 2712  
 Phe Phe Val Pro Lys Lys Ser Thr Pro Lys Val Asn Ser Val Thr Ser  
 850 855 860  
 cat ggc agc aat aaa gtg gga tca cac act tcg cag ccg cag tgg gtc 2760  
 His Gly Ser Asn Lys Val Gly Ser His Thr Ser Gln Pro Gln Trp Val  
 865 870 875 880  
 acg ggc cca tgg ctc gcc tgc tct agg acc tgt gac aca ggt tgg cac 2808  
 Thr Gly Pro Trp Leu Ala Cys Ser Arg Thr Cys Asp Thr Gly Trp His  
 885 890 895  
 acc aga acg gtg cag tgc cag gat gga aac cgg aag tta gca aaa gga 2856  
 Thr Arg Thr Val Gln Cys Gln Asp Gly Asn Arg Lys Leu Ala Lys Gly  
 900 905 910  
 tgt cct ctc tcc caa agg cct tct gcg ttt aag caa tgc ttg ttg aag 2904  
 Cys Pro Leu Ser Gln Arg Pro Ser Ala Phe Lys Gln Cys Leu Leu Lys  
 915 920 925  
 aaa tgt tagcctgtgg ttatgatctt atgcacaaag ataactggag gattcagcac 2960  
 Lys Cys  
 930  
 cgatgcagtc gtggtgaaca ggagggtctac ctaacgcaca gaaagtcattg cttcagtgac 3020  
 attgtcaaca ggagtccaat tatgggcaga atctgtcttc tgtgaccaa agaggatgtg 3080  
 cactgcttca cgtgacagtg gtgaccttgc aatatagaaa aacttggggag ttattgaaca 3140  
 tcccctggga ttacaagaaa cactgatgaa tgtaaataca ggggacattt gaagatggca 3200  
 gaactgtctc ccccttgtca cctacctctg aatagaatgt ctttaatggt 3250

INS  
CI

<210> 15

<211> 930

<212> PRT

<213> Homo sapiens

<400> 15

Met Leu Leu Gly Trp Ala Ser Leu Leu Leu Cys Ala Phe Arg Leu Pro  
1 5 10 15

Leu Ala Ala Val Gly Pro Ala Ala Thr Pro Ala Gln Asp Lys Ala Gly  
20 25 30

Gln Pro Pro Thr Ala Ala Ala Ala Ala Gln Pro Arg Arg Arg Gln Gly  
35 40 45

Glu Glu Val Gln Glu Arg Ala Glu Pro Pro Gly His Pro His Pro Leu  
50 55 60

Ala Gln Arg Arg Arg Ser Lys Gly Leu Val Gln Asn Ile Asp Gln Leu  
65 70 75 80

Tyr Ser Gly Gly Gly Lys Val Gly Tyr Leu Val Tyr Ala Gly Gly Arg  
85 90 95

Arg Phe Leu Leu Asp Leu Glu Arg Asp Gly Ser Val Gly Ile Ala Gly  
100 105 110

Phe Val Pro Ala Gly Gly Gly Thr Ser Ala Pro Trp Arg His Arg Ser  
115 120 125

His Cys Phe Tyr Arg Gly Thr Val Asp Ala Ser Pro Arg Ser Leu Ala  
130 135 140

Val Phe Asp Leu Cys Gly Gly Leu Asp Gly Phe Phe Ala Val Lys His  
145 150 155 160

Ala Arg Tyr Thr Leu Lys Pro Leu Leu Arg Gly Pro Trp Ala Glu Glu  
165 170 175

Glu Lys Gly Arg Val Tyr Gly Asp Gly Ser Ala Arg Ile Leu His Val  
180 185 190

Tyr Thr Arg Glu Gly Phe Ser Phe Glu Ala Leu Pro Pro Arg Ala Ser  
195 200 205

Cys Glu Thr Pro Ala Ser Thr Pro Glu Ala His Glu His Ala Pro Ala  
210 215 220

His Ser Asn Pro Ser Gly Arg Ala Ala Leu Ala Ser Gln Leu Leu Asp  
225 230 235 240

Gln Ser Ala Leu Ser Pro Ala Gly Gly Ser Gly Pro Gln Thr Trp Trp

INS  
C

245                      250                      255  
 Arg Arg Arg Arg Arg Ser Ile Ser Arg Ala Arg Gln Val Glu Leu Leu  
                          260                                      265                                      270  
 Leu Val Ala Asp Ala Ser Met Ala Arg Leu Tyr Gly Arg Gly Leu Gln  
                          275                                      280                                      285  
 His Tyr Leu Leu Thr Leu Ala Ser Ile Ala Asn Arg Leu Tyr Ser His  
                          290                                      295                                      300  
 Ala Ser Ile Glu Asn His Ile Arg Leu Ala Val Val Lys Val Val Val  
                          305                                      310                                      315                                      320  
 Leu Gly Asp Lys Asp Lys Ser Leu Glu Val Ser Lys Asn Ala Ala Thr  
    325                                      330                                      335  
 Thr Leu Lys Asn Phe Cys Lys Trp Gln His Gln His Asn Gln Leu Gly  
    340                                      345                                      350  
 Asp Asp His Glu Glu His Tyr Asp Ala Ala Ile Leu Phe Thr Arg Glu  
    355                                      360                                      365  
 Asp Leu Cys Gly His His Ser Cys Asp Thr Leu Gly Met Ala Asp Val  
    370                                      375                                      380  
 Gly Thr Ile Cys Ser Pro Glu Arg Ser Cys Ala Val Ile Glu Asp Asp  
    385                                      390                                      395                                      400  
 Gly Leu His Ala Ala Phe Thr Val Ala His Glu Ile Gly His Leu Leu  
    405                                      410                                      415  
 Gly Leu Ser His Asp Asp Ser Lys Phe Cys Glu Glu Thr Phe Gly Ser  
    420                                      425                                      430  
 Thr Glu Asp Lys Arg Leu Met Ser Ser Ile Leu Thr Ser Ile Asp Ala  
    435                                      440                                      445  
 Ser Lys Pro Trp Ser Lys Cys Thr Ser Ala Thr Ile Thr Glu Phe Leu  
    450                                      455                                      460  
 Asp Asp Gly His Gly Asn Cys Leu Leu Asp Leu Pro Arg Lys Gln Ile  
    465                                      470                                      475                                      480  
 Leu Gly Pro Glu Glu Leu Pro Gly Gln Thr Tyr Asp Ala Thr Gln Gln  
    485                                      490                                      495  
 Cys Asn Leu Thr Phe Gly Pro Glu Tyr Ser Val Cys Pro Gly Met Asp  
    500                                      505                                      510  
 Val Cys Ala Arg Leu Trp Cys Ala Val Val Arg Gln Gly Gln Met Val  
    515                                      520                                      525  
 Cys Leu Thr Lys Lys Leu Pro Ala Val Glu Gly Thr Pro Cys Gly Lys  
    530                                      535                                      540  
 Gly Arg Ile Cys Leu Gln Gly Lys Cys Val Asp Lys Thr Lys Lys Lys

INS  
C1

850                      855                      860  
 His Gly Ser Asn Lys Val Gly Ser His Thr Ser Gln Pro Gln Trp Val  
 865                      870                      875                      880  
 Thr Gly Pro Trp Leu Ala Cys Ser Arg Thr Cys Asp Thr Gly Trp His  
                     885                      890                      895  
 Thr Arg Thr Val Gln Cys Gln Asp Gly Asn Arg Lys Leu Ala Lys Gly  
                     900                      905                      910  
 Cys Pro Leu Ser Gln Arg Pro Ser Ala Phe Lys Gln Cys Leu Leu Lys  
                     915                      920                      925  
 Lys Cys  
                     930

<210> 16

<211> 42

<212> PRT

<213> Homo sapiens

<400> 16

Ser Ile Ser Arg Ala Arg Gln Val Glu Leu Leu Leu Val Ala Asp Ala  
 1                      5                      10                      15

Ser Met Ala Arg Met Tyr Gly Arg Gly Leu Gln His Tyr Leu Leu Thr  
                     20                      25                      30

Leu Ala Ser Ile Ala Asn Lys Leu Tyr Phe  
                     35                      40

<210> 17

<211> 23

<212> DNA

<213> Mus musculus

<400> 17

cggccacgac cctcaagaac ttt

23

<210> 18

<211> 25

<212> DNA

<213> Mus musculus

<400> 18

gcatggaggc catcatcttc aatca

25

INS  
CI

<210> 19

<211> 22

<212> DNA

<213> Homo sapiens

<400> 19

gggaggattt atgtgggcat ca

22

<210> 20

<211> 23

<212> DNA

<213> Homo sapiens

<400> 20

gtgcatttgg accagggcctt aga

23

<210> 21

<211> 13

<212> PRT

<213> artificial

<220>

<223> Synthesized peptide.

<220>

<221> MOD\_RES

<222> (12)..(12)

<223> Acp

<400> 21

Ser Ile Ser Arg Ala Arg Gln Val Glu Leu Leu Xaa Cys

1

5

10

INS  
CI